Remarks

Restriction Requirement

In response to the Restriction Requirement issued on October 24, 2008, in the above-mentioned case Applicants elect Group I, claims 1-5 and 7-10, with traverse.

The Restriction Requirement is improper and Applicants respectfully request that it be withdrawn. This restriction requirement has been issued after a first action on the merits. The M.P.E.P. states that:

> Before making a restriction requirement after the first action on the merits, the examiner will consider whether there will be a serious burden if restriction is not required.

See M.P.E.P. §811. There is no serious burden present in this case. In fact, the prior art for **all** of the pending claims has been searched and an Office Action has been issued in the application. As such, there is no burden on the Office to complete a prior art search on the claims. The M.P.E.P. states that:

> If the search and examination of the entire application can be made without serious burden, the examiner **must** examine it on the merits, even though it includes claims to independent or distinct inventions.

See M.P.E.P. § 803, emphasis added. Clearly there is no serious burden in the search of the entire application because a search of all of the claims has **already been completed** by the Office. The Office has already cited alleged prior art in an Office Action, which was clearly found in a search by the Office. Therefore, there clearly is no burden on the Office, let alone a serious burden, and the Office must examine the entire application on the merits.

The M.P.E.P. additionally states that:

> . . . the examiner should make a proper requirement as early as possible in the prosecution, in the first action if possible, otherwise as soon as the need for a proper restriction develops. See M.P.E.P. §811.

A need for a restriction has not "developed" in this case. In Applicants' last response the claims 2 and 3 were amended to state "*in vivo* induced antigen" to clarify an alleged antecedent basis issue. This clarifying amendment clearly did not cause a "need for a proper

restriction." As noted above, all of these claims have already been searched by the Office. Therefore, no need for restriction has "developed" in this case.

The Office asserts that "since the bacteria is actually a single cell organism, cell culture propagation would be considered *in vivo*; however, *in vitro* could also be interpreted as "outside" a host." The Office's interpretation of "*in vivo*" and "*in vitro*" as used in the claims is erroneous. In the field of microbial pathogenesis, the term "*in vitro*" is used to refer to single microbial cultures grown in the laboratory and *in vivo* is used to refer to microbes that are present in the host organism. *See*, for example:

1. Hautefort & Hinton, "**Measurement of bacterial gene expression *in vivo*,**" Phil. Trans. R. Soc. Lond. B. (2000) 355:601 (of record), which teaches:

> The complexities of bacterial gene expression during mammalian infection cannot be addressed by *in vitro* experiments. We know that the infected host represents a complex and dynamic environment, which is modified during the infection process, presenting a variety of stimuli to which the pathogen must respond if it to be successful. The response involves hundreds of *ivi* (*in vivo*-induced) genes which have recently been identified in animal and cell culture models. *See* abstract.

2. Chiang *et al.*, "***In vivo* Genetic Analysis of Bacterial Virulence**," Annu. Rev. Microbiol. (1999) 53:129 (of record), which teaches:

> *In vitro* assays contribute greatly to our understanding of bacterial pathogenesis, but they frequently cannot replicate the complex environment encountered by pathogens during infection. The information gained from such studies is therefore limited. *In vivo* models, on the other hand, can be difficult to use, and this has to some extent diminished the incentive to perform studies in living animals. However, several recently developed techniques permit *in vivo* examination of many genes simultaneously. *See* abstract.

3. Handfield & Levesque, "**Strategies for Isolation of *In Vivo* Expressed Genes from Bacteria**," FEMS Microbiol. Rev. (1999) 23:69 (of record), which teaches:

> The discovery and characterization of genes specifically induced *in vivo* upon infection and/or at a specific stage of the infection will be the next phase in studying bacterial virulence at the molecular level. . . . [*I*]*n vitro* systems

> initially described did not always allow the reconstruction of exact interactions between bacteria and the host. . . .[A]nimal models still represent one of the best approaches for studying *in vivo* induced (*ivi*) genes, genes defined by the process of being expressed solely *in vivo*. *See* pages 69-70.

Therefore, as evidenced by the state of the art, "*in vivo*" in not used to refer to microbes grown in single culture in the laboratory as alleged by the Office.

The Office incorrectly asserts that the common technical feature of the claims it the method step of adsorbing antibodies against *in vivo* expressed microbe antigens with *in vitro* microbe extracts and alleges that Ebersole teaches this method step. However, one common method step of the instant claims is accurately stated as "adsorbing antibodies against antigens that are expressed by the microbe *in vivo* and *in vitro* with cells or cellular extracts of the microbe that have been grown *in vitro* and isolating unadsorbed antibodies."[1] Ebersole does not teach or suggest this common technical feature.

Finally, no undue burden exists to examine all of the herein presented claims in their entirety. In particular, the claims all contain common novel technical features including, for example, "adsorbing antibodies against antigens that are expressed by the microbe *in vivo* and *in vitro* with cells or cellular extracts of the microbe that have been grown *in vitro* and isolating unadsorbed antibodies" and "probing an expression library of the microbe's DNA or RNA with the isolated unadsorbed antibodies."

The Office has not demonstrated an examination burden. Accordingly, Applicants respectfully request that claims 1-17, **which have already been examined and searched by the Office** remain as pending and be examined on the merits.

Respectfully submitted,

Dated: November 19, 2008

By: /Lisa M.W. Hillman/
Lisa M.W. Hillman, Ph.D
Registration No. 43,673
217-239-1962

[1] There are other common technical features of the claims including, for example, probing an expression library of the microbe's DNA or RNA with the isolated unadsorbed antibodies.